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A marked-up version of the amendments showing the changes made is attached hereto as **Exhibit 1.**

REMARKS

Claims 1-2, 5, 9-12, 15, 18-21, 23, and 25-31 were pending in the subject application. By this Amendment applicants have canceled claims 15, 18-21, 23, and 25-31 without prejudice or disclaimer, amended claim 5, and added new claims 37-50. Accordingly, upon entry of this Amendment claims 1-2, 5, 9-12, and 37-50 will be pending and under examination.

Applicants maintain that new claims 37-50 and the amendment of claim 5 raise no issue of new matter and are fully supported by the specification as filed. Support for amended claim 5 may be found *inter alia* in the specification as originally filed on page 16, line 35 through page 17, line 2. Support for new claims 37-38 may be found *inter alia* in the specification as originally filed on page 16, lines 26-29. Support for new claims 39-40 may be found *inter alia* in the specification as originally filed on page 17, lines 6-10. Support for new claims 41-46 may be found *inter alia* in the specification as originally filed on page 14, lines 28-32. Support for new claims 47-50 may be found *inter alia* in the specification as originally filed on page 19, line 19 through page 20, line 6. Accordingly, applicants respectfully request that the amendment be entered.

Restriction Requirement Under 35 U.S.C. §121

In the April 30, 2002 Office Action, the Examiner to whom the subject application is assigned stated that restriction to one of the following inventions is required under 35 U.S.C. §121:

I. claims 1, 2, 5, and 10-12, drawn to nucleic acids, a vector, a host cell, and a method for producing a polypeptide;

II. claim 9, drawn to polypeptides;

III. claims 15, and 18-20, drawn to an agent, a composition comprising an agent, and a method of preparing such a composition;

IV. claim 21, drawn to a method of inhibiting the activity of a mammalian LOX-1 receptor;

V. claim 23, drawn to a method of reducing the amount of a mammalian LOX-1 receptor on the surface of a cell;

VI. claim 25, drawn to a method of inhibiting the ability of an agent to bind to and activate a membrane-bound mammalian LOX-1 receptor;

VII. claims 26, 28, and 30, drawn to a method of treating a mammalian subject afflicted with a disorder; and

VIII. claims 27, 29, and 31, drawn to a method of inhibiting the onset in a mammalian subject of a disorder.

The Examiner alleged that the inventions are distinct, each from the other because of the following reasons.

The Examiner alleged that inventions I-III are unrelated. The Examiner stated that inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instance case, the Examiner alleged that the different inventions are drawn to completely different products having completely different structures and biological functions which are not interchangeable and which require non-cohesive searches and considerations.

The Examiner alleged that inventions IV-VIII are unrelated. The

Examiner stated that inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). The Examiner alleged that in the instance case the different inventions are drawn to completely different methods each having completely different method steps, using different compositions, and having completely different outcomes. The Examiner alleged that Inventions IV-VI are drawn to a method of inhibiting the activity of a mammalian LOX-1 receptor, a method of reducing the amount of a mammalian LOX-1 receptor on the surface of a cell, and a method of inhibiting the ability of an agent to bind to and activate a membrane-bound mammalian LOX-1 receptor, respectively, whereas Inventions VII and VIII are either drawn to a method of treating a mammalian subject afflicted with a disorder or a method of inhibiting the onset in a mammalian subject of a disorder. The Examiner alleged that these methods are exclusive.

The Examiner alleged that Inventions I and V are related as product and process of use. The Examiner stated that the invention can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP §806.05 (h)). The Examiner alleged that in the instance case, the nucleic acid may be used in a materially different process such as to produce polypeptides. The Examiner alleged that for the same reason, Inventions I and VII, Inventions I and VIII are related but distinct inventions.

The Examiner alleged that Inventions II and IV are related as product and process of use. The Examiner stated that the inventions can be

shown to be distinct if either or both of the following can be shown: (1) the process for using the product as can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP §806.05 (h)). The Examiner alleged that in the instance case, the polypeptide may be used in a materially different process such as to immunize mice to produce antibodies. The Examiner alleged that for the same reason, Inventions II and VI, Inventions II and VII, and Inventions II and VIM are related but distinct inventions.

The Examiner alleged that Inventions III and IV are related as product and process of use. The Examiner stated that the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP §806.05 (h)). The Examiner alleged that in the instance case, an agent may be used in a materially different process such as to determine the functions of the LOX-1 receptor. The Examiner alleged that for the same reason, Inventions III and VI, Inventions III and VII, and Inventions III and VIII are related but distinct inventions.

The Examiner alleged that Invention I is an independent invention from Inventions IV and VI; Invention II is an independent invention from Invention V; and Invention III is an independent invention from Inventions V. The Examiner alleged that the different inventions are drawn to distinct product and method inventions.

The Examiner stated that because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent

subject matter, restriction for examination purposes as indicated is proper.

The Examiner stated that because these inventions are distinct for the reasons given above and the search required for a single group is not required for any other group, restriction for examination purposes as indicated is proper.

The Examiner also stated the application contains claims drawn to different nucleic acids (SEQ ID NOS: 14, 16, 18, 22, 24, and 26) or amino acids (SEQ ID NOS: 13, 15, 17, 21, 23, 25, 27, and 28), that each individual sequence represents a structural and functionally distinct entity that is capable of supporting a separate patent, and that the search and consideration of more than a single sequence constitutes an undue search burden on the Patent Office, given the ever-increasing size of the database. The Examiner further stated that applicants are advised that a reply to this requirement must include an identification of a nucleic acid or an amino acid sequence that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The Examiner also stated that Group VII contains claims directed to patentably distinct species: (a) treating a mammalian subject using an agent that *inhibits the activity* of LOX-1 receptor; (b) treating a mammalian subject using an agent that *inhibits the expression* of LOX-1 receptor; and (c) treating a mammalian subject using a soluble LOX-1 receptor. The Examiner also stated that Group VIII also contains claims

directed to patentably distinct species: (a) inhibiting the onset in a mammalian subject of a disorder using an agent that *inhibits the activity* of LOX-1 receptor; (b) inhibiting the onset in a mammalian subject of a disorder using an agent that *inhibits the expression* of LOX-1 receptor; and (c) inhibiting the onset in a mammalian subject of a disorder using a soluble LOX-1 receptor.

The Examiner stated that should applicants elect Group VII or Group VIII, applicants are required under 35 U.S.C. §121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

The Examiner stated that upon the allowance of a generic claim, applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. §1.141. If claims are added after the election, applicants must indicate which are readable upon the elected species. MPEP § 809.02 (a).

The Examiner stated that should applicants traverse on the ground that the species are not patentably distinct, applicants should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the Examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. §103(a) of the other invention.

In response to this restriction requirement, applicants hereby

elect, with traverse, to prosecute the invention identified by the Examiner as Group I, i.e., claims 1, 2, 5 and 10-12, drawn to nucleic acids, a vector, a host cell, and a method for producing a polypeptide. Applicants maintain that new claims 37-50 are drawn to the invention of Group I. In response to the election of species requirement, applicants elect, with traverse, an isolated nucleic acid encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:14. Applicants maintain that claims 1, 2, 5, 10-12, 37-41, and 47-50 read on this species.

Applicants note that 35 U.S.C. §121 states, in part, that "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." [Emphasis added]. Applicants request that the restriction requirement be withdrawn in view of the fact that the claims of the Groups I-VIII are not independent.

Under M.P.E.P. §802.01, "independent" means "there is no disclosed relationship between the ... subjects disclosed, that is, they are unconnected in design, operation, or effect... ." The claims of Groups I-VIII are related in that they are drawn to nucleic acids encoding LOX-1 receptors, isolated LOX-1 receptor proteins, methods of inhibiting LOX-1 receptors, and methods of treatment comprising inhibiting LOX-1 receptors. In particular, Group I is drawn to nucleic acids and Group II is drawn to proteins.

Applicants therefore respectfully assert that two or more independent and distinct inventions have not been claimed in the subject application because the groups are not independent under M.P.E.P. §802.01.

Additionally, applicants point out that under M.P.E.P. §803, the Examiner must examine the application on the merits, even though

it includes claims to distinct inventions, if the search and examination of an application can be made without serious burden. There are two criteria for a proper requirement for restriction, namely (1) the inventions must be independent and distinct; AND (2) there must be a serious burden on the Examiner if restriction is not required.

Applicants maintain that there would not be a serious burden on the Examiner if restriction were not required. A search of prior art with regard to any one of Groups I-VII would necessarily identify art for another Group. Since there is no serious burden on the Examiner to examine Groups I-VIII in the subject application, the Examiner must examine the entire application on the merits.

Accordingly, in view of the preceding remarks, applicants respectfully request that the Examiner reconsider and withdraw the requirement for restriction.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone the number provided below.

No fee, other than the enclosed $209.00 fee ($9.00 filing fee plus $200.00 for a two month extension of time), is deemed necessary in connection with the filing of this Amendment. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

7/26/02

Alan D. Miller Date
Reg. No. 42,889

Marked-up Version of Amendments Showing Changes Made

Additions to the text are indicated by underlining; deletions are indicated by square brackets.

--5. (Amended) A nucleic acid probe of at least [about] 15 nucleotides in length which specifically hybridizes with a nucleic acid <u>of claim 1</u> encoding a mammalian LOX-1 receptor or with a nucleic acid having the complementary sequence thereof.--

EXHIBIT 1
Alan R. Tall et al.
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